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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/788,825	02/27/2004	Lifen Shen	LA0100 (NP)	6942

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EXAMINER

KRISHNAN, GANAPATHY

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 02/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/788,825

Applicant(s)

SHEN ET AL.

Examiner

Ganapathy Krishnan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-27 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on ____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 5/10 and 6/16, '04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Claim Objections

Claim 15 is a duplicate of claim 1. It should be cancelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4-8, 10, 13-15 and 18-20 recite the term non-cryogenic. It is not clear what temperature range is considered non-cryogenic. This must be defined in the claim. For the purpose of prosecution temperatures below zero degrees will also be considered non-cryogenic. Claims 1 and 15 recite, "a carbonyl-substituted reactant to form a glycoside". It is not clear what applicants intend by this recitation because not all carbonyl-substituted reactants will form a glycoside on reaction with a lithiated anionic species. Claims 1 and 15 recite the term microreactor. This term is interpreted as any standard glassware used in a laboratory to perform lithiation and coupling reactions as instantly claimed.

Claims 8 and 19, which depend from claims 1 and 15 respectively, recite cryogenic conditions but claims 1 and 15 are drawn to a non-cryogenic process. It is not clear what

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applicants intend by the recitation of claims 8 and 19. For the purpose of prosecution cryogenic conditions is interpreted as any temperature below 26°C used in the said process.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 5, 7, 8, 14, 15, 20, 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Czernecki et al (J. Org. Chem. 1991, 56, 6289-6292).

Czernecki et al teach the reaction of a carbonyl-substituted compound (1) with the lithiated aromatic compound (3a or 3b) to form the glycoside 5 and 8 (see scheme II, page 6290). The lithiated aromatic anionic species is prepared by reacting the aromatic compound 2a or 2b (aromatic halide) wherein bromine (a halide) is the leaving group (Scheme I, page 6289, bottom right). This teaching meets the limitations of claims 1, 5, 8, 15, 21 and 22. The glycoside 8a is hydrogenated to remove the benzyl protecting group to give the glycoside 9a in 98% yield (Scheme II, page 6290; page 6291, right column, see second full paragraph- Preparation of compound 9a). This meets the limitations of claim 7, 14 and 20.

Joint Inventors

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

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commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4, 6, 9-13, 15-19 and 23-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Czernecki et al (J. Org. Chem. 1991, 56, 6289-6292) in combination with Hawley's Condensed Chemical Dictionary, 13th Edition, 1997, page 180 and Grant and Hackh's Chemical Dictionary, 5th edition, 1987, page 436.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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Claims 1 and 15 are drawn to a process of making a glycoside using a non-cryogenic process comprising lithiating an aromatic reactant having a leaving group using a lithium reagent to form a lithiated anionic species and coupling the lithiated anionic species with a carbonyl substituted reactant to form a glycoside. Dependent claims 2-4, 9-13 14-19 and 23-27 recite process limitations drawn to temperature time of reaction, lithiating reagent and solvents used in the process.

Czernecki et al teach the reaction of a carbonyl-substituted compound (1) with the lithiated aromatic compound (3a or 3b) to form the glycoside 5 and 8 (see scheme II, page 6290). The lithiated aromatic anionic species is prepared by reacting the aromatic compound 2a or 2b (aromatic halide) wherein bromine (a halide) is the leaving group (Scheme I, page 6289, bottom right). Czernecki teaches the use of both THF and toluene in the process (page 6290, left column, last paragraph through page 6290, right column line 15). Czernecki teaches the lithiation step as well as the coupling step at low temperatures, namely -78°C and -40°C . In Table I (at page 6290) Czernecki discloses the use of toluene, petroleum ether and THF. It is seen in the same table that the formation of the compound 4 predominates. Compound 4 is obtained via the hydrolysis of the corresponding lithiated species 3 (See Scheme I, page 6289). This result indicates that in these solvents a very high percentage of the lithiated anionic species is formed, which when coupled to the carbonyl substituted compound would give a higher yield of the desired glycoside. From Table I it can also be seen that the required species 3 is formed in greater amount even at higher temperatures since the corresponding hydrolysis product 4 is obtained in higher yield.

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Even though Czernecki et al teach the use of sec-butyl lithium, one of ordinary skill in the art knows that n-butyl lithium and t-butyl lithium are both used in lithiation reaction routinely in organic synthesis as a metalating agent (see Hawley's Condensed Chemical Dictionary, page 180, under the title-butyllithium). It is also well within the purview of one of ordinary skill in the art to vary process conditions like temperature. The use of mixtures of aprotic solvents and heptane as instantly claimed are also obvious variants. Heptane is very similar to petroleum ether (used by Czernecki), which is a mixture of pentanes and hexanes (see Table 61, page 436, Grant & Hackh's Chemical Dictionary). This fact is also well known to one of ordinary skill in the art.

Based on this teaching of the prior art it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a non-cryogenic process comprising forming a lithiated anionic species and coupling it with a carbonyl substituted compound to form a glycoside as instantly claimed since the reagents, process steps and conditions are seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to vary the temperature and substitute sec-butyl lithium with other agents like n-BuLi and t-BuLi and also substitute solvents in order to optimize the process. According to Czernecki the formation of the lithiated anionic species is greater in petroleum ether (which is similar to heptane) and toluene, which in turn would lead to a higher yield of the glycoside in the subsequent coupling step.

Conclusion

Claims 1-27 are rejected

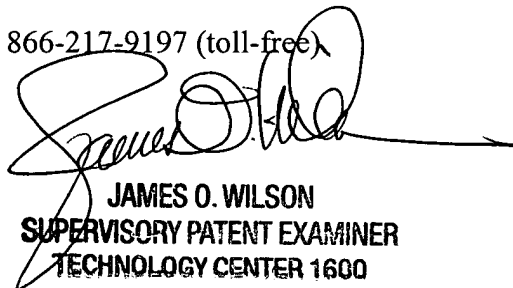
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached between 8.30am-5.00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GK



JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
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